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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/688,090 | 10/17/2003 | Rubinah K. Chowdhary | 273012011601 | 9064 |

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| EXAMINER | |
|---|---|
| FUBARA, BLESSING M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1618 | |

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/688,090 | CHOWDHARY ET AL. | |
| | Examiner | Art Unit | |
| | Blessing M. Fubara | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,7-14,18,19 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-14,18,19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Examiner acknowledges receipt of remarks and amendment after final rejection. Claims 1, 7-14, 18, 19 and 21 are pending.

1. Applicants' request for reconsideration of the finality of the rejection of the last Office action is withdrawn since the prior art of record does not specifically disclose solid form. However, the prior art references of record are applicable under 35 USC 103 and the rejection below is made.

### *Claim Rejections - 35 USC § 112*

The rejection of claim 21 under 35 USC 112, first paragraph as containing New Matter is withdrawn in light of applicants' persuasive argument.

The rejection of claim 7 under 35 USC 112, second paragraph as being indefinite is withdrawn in light of applicants' persuasive argument.

The restrictive requirement made in the final rejection is withdrawn in light of applicants' argument.

2. Claims 7 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description for the transition phases between the preceding phases that are between micelles, emulsions, gels and matrix. There is also no description or definition for FC43, PP11 and PP25 in claim 18.

3. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. It is not clear what phases are being referred to. Is the transition phase between the micelle and the emulsion or gel or matrix; it is not clear if the transition state is between the micelle and all the other phases. The claims do not further define the transition states.

***Claim Rejections - 35 USC § 102***

4. Claims 1, 7, 8, 10-14, 18 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Richter et al. (US 6,274,614).

Richter discloses composition comprising photosensitizing agent and absorbent applicator (abstract) and physiologically acceptable carriers (column 12, lines 13-17). The photosynthesizing agent can be administered as liquid, gel or gelatinous solid pharmaceutical composition (column 17, lines 32-34). Poloxamer surfactants are suitable and specifically, when fluorocarbons are used, PLURONIC F-68 is used with perfluorodecalin (column 18, line 65 to column 19 line 6); Richter specifically discloses that lyophilized formulation is suitable for storage (column 19, lines 10-16). Lyophilizing the emulsion would form a solid and would meet the limitations of a solid formulation. Green porphyrines and derivatives are examples of the photosensitizing agent used in Richter (column 11, line 38 to column 17 line 10); the chlorine system is also used (column 14, line 66 to column 15 line 3). A sponge is saturated with the photosensitizer containing liposomal BPD (a hydromonobenzoporphyrin derivative) and the BPD saturated sponge is placed in contact with the tissue to be treated (column 22, lines 17-25). Claim 21 reads on the BPD saturated sponge, the solid support reading on the sponge. Richter does not disclose polystyrene polymer and does not disclose the use

of poloxamer 188 when fluorocarbons are not used; specifically discloses poloxamer 188 or Pluronic F 68 for use with perfluorodecalin. Richter does not include FC43, PP11 and PP25 fluorocarbons in the composition.

***Claim Rejections - 35 USC § 103***

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajagopalan et al. (WO 99/51284), reference provided by applicants in Form PTO 1449.

Rajagopalan teaches a composition that comprises non-covalent carrier-hapten complexes of the structure HM----CM, where HM is the hapten and is selected from the group consisting of peptides, carbohydrates, **photosensitizers** and fluorescent dyes; and CM is a carrier molecule where surfactant is one of the carrier molecule (claim 1). Rajagopalan specifically teaches that the photosensitizer has absorption and emission maxima in the range of 200-1200 nm (claims 2, 4, 10, 12 and 18). HM is further selected from the group consisting of cyanine, indocyanine, squaraine, porphyrins, Rose Bengal and methylene blue (claims 6, 15, 22 and 29). CM is a surfactant (claims 5, 8, 11, 13, 17, 19, 21, 24 and 26), polyaspartic acid (claims 7, 16, 23 and 30), and polyaspartic acid is one of the block copolymers recited in claim 8. Rajagopalan administers the non-covalent carrier-hapten bioconjugate to a patient for diagnostic or therapeutic procedure where the procedure is selected from the group consisting of tomographic imaging, fluorescence and absorbance monitoring and endoscopic examinations (claims 8 and 9). Rajagopalan teaches that the hapten is preferably a photosensitizer, which is capable of transferring energy to tissues or to other components

inside and outside the cell (page 6, lines 13-15). The composition of Rajagopalan is a solution or liquid or sterile aqueous solution or suspension (page 8, lines 8-18)

Rajagopalan discloses a liquid composition comprising a photosensitizer and block copolymer where the block copolymer is not a poloxamer 188 or amphiphilic polymer of polystyrene sodium sulphonate and vinyl naphthalene. Rajagopalan's formulation is not a solid. But the formulation of Rajagopalan is used in diagnostic and therapeutic therapy. There is no demonstration in applicants' specification that using a solid form of the photosensitizer in the block copolymer emulsion provides unusual results. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the formulation of Rajagopalan for diagnostic and therapeutic therapy with the expectation that the formulation would be effectively used in optical tomographic imaging procedure. In the absence of a showing a solid formulation is not inventive over liquid or suspension where both the suspension and the solid contain photosensitizer and block copolymer.

7. Claims 1 and 7-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lyons (US 5,616,342).

Lyons teaches an emulsion composition that comprises surfactant, co-surfactant and pharmacologically and photoreactive photosensitizing compound and specifically pyrrole-based macrocyclic compounds. The photosensitizing compounds of interest in Lyons are natural or synthetic porphyrins, chlorines, and bacteriochlorins, synthetic isobacteriochlorins, phthalocyanines, naphthalocyanines, porphycenes, sapphyrins and texaphyrins and derivatives thereof. Lyons' emulsion composition is utilized in oxygen-dependent and oxygen-independent phototherapy, and the emulsion is capable of being

autoclaved. See column 1, lines 9-22, column 2, lines 37-62 and columns 3-7, and claims 20, 21 and 23.

Lyons composition further comprises oils (column 8, lines 1-16) and stabilizer selected from phosphatides, soybean phospholipids, and non-ionic poloxamer block-copolymers, synthetic or semi-synthetic phospholipids with egg yolk phospholipid, the preferred stabilizer (column 8, lines 17-26). The composition further comprises isotonic agents, auxiliary ingredients and solvents (column 8, lines 47-67).

Lyons teaches a method for diagnosing a patient for tumor wherein the method comprises administering the emulsion composition to said patient and then exposing the patient to light that has a suitable wavelength to induce fluorescence of photosensitizing compounds that are maintained by abnormal cells (claim 28). In claims 25 and 27, the emulsion of Lyons is administered to a patient, after which the patient is exposed to light to activate the photosensitizing agent in the emulsion, to treat said patient. No unexpected result is presented for use of solid vs. emulsion formulations, both of which are used in photodynamic therapy.

Lyons clearly teaches the composition and the method for conducting photodynamic therapy except that the broad teaching of poloxamer encompasses all forms of poloxamers including poloxamer 188. Thus the expected composition is one that comprises photosensitizing agents, poloxamer block copolymer that may include or exclude poloxamer 188, oil as emulsion forming agent and auxiliary ingredients and solvents for administration to a patient for photodynamic therapy. There is no suggestion in the prior art that poloxamer 188 would be preferred in the composition of the prior art. Therefore, it would have been obvious to one of ordinary skill in the art at

the time the invention was made to prepare the photosensitizer composition of the prior art where the broad teaching of poloxamer encompasses all poloxamers. One having ordinary skill in the art would have been motivated to prepare an emulsion composition comprising photosensitizing agents and poloxamer that may include or exclude poloxamer 188. In the absence of a showing of unexpected result of excluding poloxamer 188, the claims in the application are not inventive over the prior art.

8. Claims 18 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lyons (US 5,616,342).

Lyons is discussed above. Lyons discloses a composition that has a broad teaching of poloxamers. There is no suggestion in Lyon to exclude poloxamer 188. In Lyon, oil is an emulsion-forming agent; oil is not a fluorocarbon. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the photosensitizer composition of the prior art where the broad teaching of poloxamer encompasses all poloxamers. One having ordinary skill in the art would have been motivated to prepare an emulsion composition comprising photosensitizing agents and poloxamer that may include or exclude poloxamer 188. It is within the purview of the person of ordinary skill in the art to remove solvent in order to form a solid. In the absence of a showing of the criticality of including poloxamer 188, the claims in the application are not inventive over the prior art.

1. The prior art made of record and not relied upon is considered pertinent to applicants' disclosure.

Stewart et al. (WO 98/34644, provided by applicants in Form PTO 1449) discloses a composition comprising a photosensitizing agent and one or more

physiologically acceptable carriers (page 28, lines 21-28). The photosensitizing agent is administered alone or with water or other pharmaceutically acceptable excipients in a liquid, gel or gelatinous composition (page 29, lines 7-24). The photosensitizing composition comprises a poloxamer surfactant block copolymer (page 31, lines 25-27). Stewart's photosensitizing agents are benzoporphyrin compounds selected from BPD-MA, BPD-MB, BPD-DA and BPD-DB (page 27, line 9 and claims 4 and 21). Stewart discloses a method of reducing or preventing the effects of inflammation that results from injury to tissues and the method comprises the steps of contacting the injured tissue with the photosensitizing composition and exposing the treated tissue to light of the appropriate energy to photodynamically treat the injured tissue (abstract, page 1, lines 5-15). Stewart further discloses that the photosensitizing agent may be combined with one or more immunosuppressive agents to enhance the anti-inflammatory effect of the photosensitizing agent (page 30, lines 10-13). The poloxamer block copolymer of Stewart encompasses all form the poloxamer. The emulsion-forming agent is a fluorocarbon.

***Response to Arguments***

Applicants state that the prior art formulations are not solid formulations. However, the prior art formulation and the instant formulation are both radiation sensitive formulations. There is no demonstration that the use of solid has unexpected results over the use of liquid or emulsions and the person of ordinary skill in the art has the technical know to remove solvent to form a solid.

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicants may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600